REMARKS

Claims 1, 4, 7, 8, 11-14, 20, 21, 23-27, 29-32, 37-41 and 51-59 are in the application. Claims 1, 11, 12, 21, 52-55 and 57- 59 have been amended. Support for the amendments lies in the claims as originally filed, to correct typographical errors, or to better define and claim the invention. No new matter is believed added.

The amendments to the specification are to correct an obvious typographical error.

Claims Objections

Claims 11, 21 52-54, 57-58 are objected to by the Examiner.

Claim 11 has been amended to recite claim dependency on Claim 1.

Claims 21, 52-54, and 57-58 have been amended to delete the duplicate subject matter. Claim 58 is also amended to recite claim dependency upon Claim 57. The Examiner is thanked for his attention to these typographical errors.

Rejection under 35 USC §112, 2nd Paragraph

Claims 12, 13 and 59 are rejected under 35 USC §112, 2nd paragraph as failing to point out and distinctly claim the invention.

Claim 12 and 13 recite limitations not present in amended Claim 1. Claim 1 has been amended to recite the limitation of original claim 10. This should remove the rejection to Claims 12 and 13.

Claim 59 has been amended to recite the examples in the alternative, all of which as noted by the Examiner are formulations within the content of Claim 1.

Reconsideration and withdrawal of the rejection to the claims under 35 USC §112 is respectfully requested in view of the amendments herein.

Rejection under 35 USC §103

Claims 1, 4, 7, 11-14. 20-21, 23-25, 27, 29-32, 37-41 and 51-59 stand rejected under 35 USC §103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190). Applicants respectfully traverse this rejection.

Claims 8 and 26 stand rejected under 35 USC §103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190) and De Bock et al. (US 5, 428, 150). Applicants also respectfully traverse this rejection.

The Breitenbach et al. patent is directed to a tablet which comprises as the foaming polymer **a thermoplastic polymer** selected from a water-soluble, melt processable homo or copolymer of N-vinylpyrrolidone or mixtures of such polymers (see Column 2, lines 58-60). Claim 1 requires a thermoplastic polymer to be present.

The Examiner comments that Claim 1 of the instant application uses the open ended construction "comprising" as shown in the excerpt from page 3 of the Office Action:

> This is not persuasive because instant claims recite the transitional phrase "comprising" which is open language and does not exclude other polymers. Breitenbach also teaches foamed active ingredient preparations comprising bulking agents (mannitol, sorbitol, xylitol) which are the non-thermosetting polymerized plastics material of instant claim 1. Breitenbach teaches starch which is the non-thermosetting modifier.

This is clearly missing that point that the Breitenbach et al. invention requires the use of a thermoplastic polymer. All the additional excipients taught in Breitenbach are just that, additional excipients.

Applicants do not require a thermoplastic polymer.

It is clear from the Applicants specification that the purpose of the claimed invention is that the behavior of a thermoplastic polymer can be obtained without the need for including such a polymer. Consequently, the claim is not directed to this.

Claim 1 as previously amended requires a specific polyol and non-thermosetting modifier and/or non-thermosetting polymer. In direct contrast to this the Breitenbach et al. patent requires a thermoplastic polymer, such as N-vinylpyrrolidone. However, Applicants have further amended claim 1, in order to advance prosecution on the merits

to include in the body of the claim, the preamble which requires that the "molded microcellular polymeric material and pharmaceutically active agent are injection molded into a pharmaceutical dosage form". This further distinguishing Applicants claimed invention over the Breitenbach et al. patent.

The MPEP, under section 706.02 clearly directs the Examiner to the criteria necessary for a rejection under 35 USC §103:

706.02(j) Contents of a 35 U.S.C. 103 Rejection [R-6]

35 U.S.C. 103 authorizes a rejection where, to meet the claim, it is necessary to modify a single reference or to combine it with one or more other references. After indicating that the rejection is under 35 U.S.C. 103, the examiner should set forth in the Office action:

(A) the relevant teachings of the prior art relied upon, preferably with reference to the relevant column or page number(s) and line number(s) where appropriate,

(B) the difference or differences in the claim over the applied reference(s),

(C) the proposed modification of the applied reference(s) necessary to arrive at the claimed subject matter, and

(D) an explanation >as to< why >the claimed invention would have been obvious to< one of ordinary skill in the art at the time the invention was made**.

**

"To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). **

In the present instance the Examiner has not established any reason under points B) and C) above, that the present invention would be obvious over the cited art of Breitenbach et al. patent, whether or not in view of any secondary references. The claims

of the present invention simply do not use a thermoplastic polymer. There is no "proposed modification of the applied reference" under any circumstance that could be used to arrive at Applicants claimed subject matter. There is "no proposed modification of the applied reference" taken with any of the secondary references, under any circumstances, that could be used to arrive at Applicants claimed subject matter.

The explanation provided by the Examiner is simply that Breitenbach et al. optionally includes some of the excipients defined as a non-thermosetting modifier herein. But for what reason, and even if added does still not achieve Applicants formulation, nor the requirement that the formulation be injection molded.

The Examiner also comments in the Office Action, on page 3, last paragraph that:

> Applicant argues that a significant difference between the present invention and Breitenbach et al. is that microcellular foam tablets of the present invention are formed in-situ, by first intent, in a novel injection molding process (as described herein). Applicant argues that Breitenbach et al. prepares thermoplastic foam extrudates in a conventional extruder, the extrudates are then shaped into forms by secondary processes, i.e., cutting, chopping, punching (see column 5, lines 31 to 61). Applicant argues that consequently, the formulation and the process of using this formulation to make injection molded tablets is fundamentally different.
>
> This is not persuasive because instant claims are drawn to a composition and do not recite any product-by-process or process limitations. The components of the composition are taught by the prior art references and the specific limitations are rendered obvious by the combination of Breitenbach and Jane.

The Examiner is correct that the Applicants claims are drawn to a composition, and are not a product by process claim. However, the composition is still read in light of the specification regardless. Applicant's specification clearly teaches one skilled in the art how to utilize the claimed composition to produce a molded microcellular dosage form. The skilled artisan would recognize that the simple mixtures of Breitenbach cannot

attain the same degree of microcellular foam structure of the present invention, which is a unique feature of this invention and required by Claim 21 specifically.

Therefore, the limitations of Applicants Claim 1 are not taught nor disclosed by the Breitenbach et al. patent. Going further, the limitations of independent Claim 21 are also not taught nor disclosed by the Breitenbach et al. patent. There is simply no motivation present in this reference to direct the skilled artisan to make the necessary modifications to prepare a composition having the particular uniform, maximum void dimensions of a microcellular form. The secondary references fail to supply the necessary motivation as well.

Claim 21, and those dependent thereon, as shown in part below, requires a **rigid microcellular foam** which is not taught nor suggested by the Breitenbach et al. disclosure as the process and compositions used in the Breitenbach et al. disclosure will not produce such as dosage form. Therefore, as with the rejection to independent claim 1 and those dependent thereon, the USPTO has failed to establish a case of obviousness under 35 USC §103.

> Claim 21 recites: "A pharmaceutical dosage form comprising: **a rigid microcellular foam consisting of a solid excipient having voids of substantially uniform size with a maximum void dimension in the range from about 2 to 100 microns and a void fraction in the range of about 5 to 95 percent,** the solid excipient comprising an active pharmaceutical agent combined in a homogeneous solid mixture with a non-thermosetting polymerized plastic material comprised of at least one polyol selected from lactitol, xylitol, sorbitol, erythritol, maltitol, or mannitol, or combinations thereof; and ....."

The present invention is the novel combination of agents which when prepared in a manner as described in the specification produce a microcellular foamed tablet containing an active pharmaceutical agent.

As previously discussed, there is a significant difference between the present invention and the Breitenbach et al. disclosure in that the microcellular foam tablets of the present invention are formed in-situ, by first intent, in a novel injection molding process. Breitenbach et al. prepares thermoplastic foam extrudates in a conventional extruder. The extrudates are then shaped into forms by secondary processes, i.e., cutting, chopping, punching (see column 5, lines 31 to 61). Consequently, the formulation and the process of using this formulation to make injection molded tablets will be, and is, fundamentally different. What reason exists to make the necessary modifications to the formulation if the use of that formulation is different?

Claim 23 recites a further limitation in which the voids of the microcellular foam are in the form of closed cells. The Breintenbach et al. patent does not teach nor suggest this result from their pharmaceutical dosage form. This result is not achieved by combining the teachings of the Breintenbach et al. patent with the secondary references.

Claim 40 of Applicants requires that the rigid microcellular foam is enclosed within a skin having a density substantially greater than that of the microcellular foam, but having the same composition as that of said solid mixture.

Again this limitation is not taught nor suggested by the Breintenbach et al. patent alone or in combination with the secondary references.

Claim 41 requires the overall density of the dosage form to be substantially less than that of stomach fluids, whereby the dosage form is gastro-retentive.

Again this limitation is not taught nor suggested by the Breintenbach et al. patent alone or in combination with the secondary references.

The Breintenbach et al. polymers are classic polymeric thermoplastic materials. In contrast, the presently claimed invention employs the novel use of thermosetting agents, such as polyols in combination with one or both of a non-thermosetting modifier and a non-thermosetting polymer. The non-thermosetting modifiers are

selected from starch, maltodextrin, a dextrose equivalent, polyalditol, or a hydrogenated starch hydrosylate, or mixtures thereof.

The non-thermosetting polymers are selected from carboxymethyl cellulose sodium, methyl cellulose, ethylcellulose, hydroxyethylcellulose (HEC), hydroxypropylmethyl cellulose (HPMC), hydroxypropylmethyl cellulose phthalate, cellulose acetate phthalate, noncrystalline cellulose, starch and its derivatives, and sodium starch glycolate or mixtures thereof.

The fact that you can produce a composition that can be injection molded into foamed tablets **despite the fact they are not thermoplastic** is an **unexpected and a novel invention.**

This novelty is not taught nor disclosed by the prior art.

The Breintenbach et al. formulations are simple mixtures that cannot attain the degree of microcellular foam structure required by Claim 21 of the present invention, also a unique feature herein. This failure is not remedied by the secondary references either.

In summary, Breintenbach et al. discloses an extrusion process to prepare foams that require further processing (like standard compression into tablets) to turn them into something useful. The present invention provides for injection molded tablets that are different from that obtained by the cited references herein.

Consequently, the Breitenbach et al. reference does not teach the specific combination of a polyol and the non-thermoplastic polymer and/or modifier as the matrix of the resulting tablet. The fact that applicants utilize the term "comprising" is still irrelevant to the fact that the primary reference does not provide the elements of Applicants invention such that the USPTO can not establish a valid rejection of the claims under the obviousness provisions of 35 USC 103.

The secondary reference, Jane et al. does not remedy the lack of teachings in the Breitenbach et al reference. The Jane reference discloses a thermoplastic composition based upon a soy protein. Jane et al. provides for additional excipients which can include other fillers and plasticizing agents, but again still requires as the basic polymer, a soy protein. The Jane reference fails to supply the necessary motivation to direct the skilled artisan to modify the teachings of the Breitenbach et al. patent to achieve the invention as claimed herein. There is no disclosure in Breitenbach alone or taken with the Jane reference that teaches the specific combination of a polyol and the non-thermoplastic polymer or modifier as the matrix of the resulting tablet.

The other secondary reference, De Bock et al. (US 5, 428, 150) teaches a starch based formulation which can be **extruded,** not injection molded, as required by amended Claim 1. There is no disclosure of this composition being used with a supercritical fluid to form a microcellular foam product. The only disclosure is to combine the composition with a thermoplastic polymeric material (column 5, lines 9-13).

A composition is not used in the abstract, it is formulated with an end use in mind. It is still read in light of the specification. In Applicants case the formulation is injection molded, not extruded into a dosage form. That limitation from the preamble of Claim 1 has been added to the body of Claim 1.

Similarly, Claim 21 as noted above requires a rigid microcellular foam structure having particular characteristics. That structure can not be achieved by the teachings of the De Bock et al. patent.

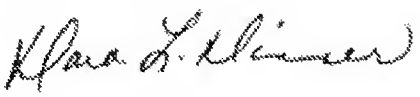
As noted previously, the De Bock et al. does not teach, nor suggest, the inclusion of an active pharmaceutical agent in the resulting article. There is no teaching or suggestion to turn the compositions of DeBock et al. into a pharmaceutical dosage form. Consequently, neither Breitenbach et al. in combination with Jane et al. or De Bock et al. provides the limitations of Claim 1 nor of Claim 21 herein.

In view of these remarks and amendments, reconsideration and withdrawal of the rejection to the claims under 35 USC §103 is respectfully requested.

CONCLUSION

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. If any additional fees or charges are required by this paper the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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